How to Quantify Hepatic Fibrosis from Different Viewpoints

SY04-1

Pathologic quantification of hepatic fibrosis

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By means of liver biopsy in cirrhosis, several different kinds of information such as diagnosis of cirrhosis, assessment of cause, fibrosis staging, inflammatory activity and detection of hepatocellular carcinoma can be obtained. Liver biopsy tissue is stained usually by H&E, Masson trichrome and Reticulin for assessment of staging and inflammatory activity.

The histological features of fibrosis development in liver tissue can be different according to causing disease of cirrhosis. In general, it has been known two different histological features of fibrosis development.

Fibrosis starts to develop in portal and periportal area as for viral hepatitis and others, and in perivenular & perisinusoidal area as for nonalcoholic steatohepatitis. Therefore, two different staging system for cirrhosis have been used.

Two major staging system for cirrhosis caused by viral hepatitis and others were proposed by Knodell and Ishak. But the one was too simple and the other was too complicated to apply to practice. For this reason, members of Gastrointestinal Pathology Study Group of Korean Society of Pathologist proposed a staging system in 1999 as follow; stage 1] no fibrosis, stage 2] portal fibrosis, stage 3] septal (bridging) fibrosis, stage 4] cirrhosis. This classification has been used in Korea until now.

The most popular staging system for cirrhosis caused by nonalcoholic fatty liver disease including NASH was proposed by Kleiner at al of the Nonalcoholic Steatohepatitis Clinical Research Network in 2005. Their classification is as follow; Stage 1] Zone 3 perisinusoidal/pericellular fibrosis; (1A] Mild, 1B] Moderate, 1C] Portal/periportal), Stage 2] Zone 3 perisinusoidal/pericellular fibrosis with focal or extensive periportal fibrosis. Stage 3] Zone 3 perisinusoidal/pericellular fibrosis and portal fibrosis with focal or extensive bridging fibrosis. Stage 4] Cirrhosis.

Despite usefulness and subtlety of liver biopsy for cirrhosis staging, it has some limitation also. To make diagnosis, the sample may be sufficiently big, and the nodules sufficiently small. On the other hand a slender core from within a large cirrhotic nodule can be difficult to identify stage. If underestimating the stage of fibrosis is a concern, correlation with clinical and laboratory data helps overcome this problem.

Keywords : Liver, Fibrosis, Stage, Quantification

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Principles and techniques of shear wave ultrasound elastography

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It is well known that changes in tissue mechanical properties, such as hardness or stiffness are possible disease markers. Thus, manual palpation has been used to assist in diagnosis. In 1991, modern digital palpation, named compressional elastography (also known as strain imaging), was introduced, which utilizes a comparison of ultrasound B-scan RF data from tissue before and after a compression. Most ultrasound machine manufactures have been commercializing this technique and it has been widely used for cancer detection. Despite its wide usage, it has been shown to be subjective and experience dependent and its use is restricted to larger and more superficial structures.

Shear Wave Elastography (SWE) is an emerging technology to overcome the drawbacks of the previous methods. The most promising merit of it is that it can provide quantitative measurements of tissue stiffness. The map of shear modulus or shear wave speed is displayed using a color coded image superimposed on the B-mode image.

Fink et al. proposed a transient shear wave elastography, named Supersonic Shear Imaging (SSI), which measures the speed of shear wave propagation traveling through human tissue. This technique uses an ultrafast ultrasound acquisition imaging system (over 5000 frames/sec) which enables the real-time visualization of transient shear wave propagation in human body. This method has been commercialized by SuperSonic Imagine, Inc. and is gaining popularity among radiologists.

Fig. 1 shows the concept of the typical shear wave elastography which consists of three steps: shear wave excitation, the measurement of shear wave propagation, and shear modulus reconstruction. To excite a shear wave, an array transducer focuses ultrasound beams at a focal point within human tissue. Acoustic radiation force is generated and pushes the tissue downward (depth direction in the figure). Then, shear waves propagate along the lateral (width) direction with the speed of 1~10 m/s. In the measurement step, plane waves are transmitted from the transducer and the echo signals are detected and saved in local memories. Plane wave imaging is used to achieve ultrafast measurements (over 5000 fps) enough to track and record the shear wave propagation. The displacement images are calculated from the recorded images using 1D cross correlation between a reference frame and one of the recorded images. In the shear modulus reconstruction, shear wave speed (*Cs*) is obtained by solving the wave equation or the cross correlation method. Then shear modulus can be calculated by $G = \rho \times C_s^2$ where G is shear modulus, ρ is the density of medium, and *Cs* is the shear wave speed. After the shear modulus reconstruction is performed on the every pixel of ultrasonic field of view, an elasticity image is generated with the shear modulus color coded.

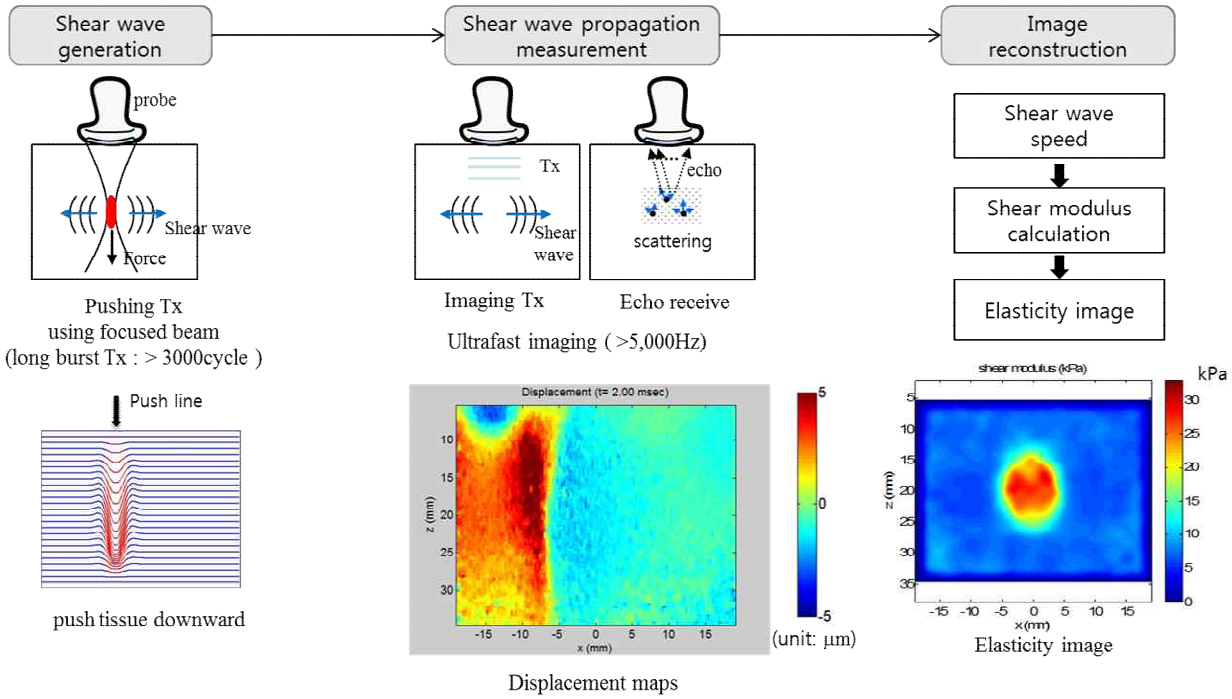

Fig1. Overview of shear wave elastography using ultrasound

Keywords : Ultrasound, Shear wave, Elastography, Stiffness, Acoustic radiation force

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CT Quantification: Liver Tissue Assessment by Dual Energy CT with Multi-Material Decomposition

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Assessing the severity of liver fibrosis has direct clinical implications for patient diagnosis and treatment. While liver biopsy is accepted as the gold standard, its result is often disputed due to the sampling error. Furthermore, its clinical utility is often questioned since it is an invasive procedure. Therefore, several imaging-based techniques for staging liver fibrosis have emerged, such as magnetic resonance elastography (MRE) and ultrasound elastography (USE), but they face challenges that include limited availability, high cost, poor patient compliance, low repeatability, and inaccuracy.

Current Computed Tomography (CT) based techniques for liver fat which is one important factor quantify based on the Hounsfield-unit (HU) relies on the fact that there is an inverse relationship between liver fat content and liver attenuation. Ultimately, semi-quantitative is remained in nature due to heuristically inferred liver fat concentration.

Dual energy CT (DECT) has been coming under the spotlight again last several years because recent CT systems have gotten an enough ability to apply Dual Energy acquisition for routine clinical use. With the nature of DECT, material quantification is more expected than conventional single energy CT (SECT). The single-source fast kV switching dual-energy method can use spatial and temporal coincident low and high energy data with clinically enough energy separation between two energies. Therefore, more accurate tissue types separation and quantification is expected. One typical imaging method in DECT is material decomposition. This decomposes into specified two materials (material pair) and can scale with the material density by accurate beam hardening correction with the two materials under the projection-space data operation process. In theory, once beam hardening in the two material data (basis pair data) is corrected respectively, these two material density images can be generated, following quantitative imaging and calculation methods such as Monochromatic imaging and Effective-Z calculation can be also generated.

These imaging methods have quantification capability, however liver tissue is composed from several different materials like native tissue, fat, iron, and Iodinated contrast material is injected in the multi-phase liver scan, thus two material separation/density images may not be enough for assessing different types of liver tissue.

We therefore developed multi-material decomposition (MMD), a flexible, model-based method that extends DECT's core material discrimination capability to allow for the disambiguation of a larger number of materials with introducing a biologically driven hypothesis. This calculates multi-material volume fractions for each image pixel based on the response of dual energy images. This method which has great potential for quantitative assessment of the liver fat and fibrosis will be discussed for future clinical application.

Keywords : CT, Dual Energy CT, Material Decomposition